REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in view of the following remarks and pursuant to 37 C.F.R. § 1.112, are respectfully requested. By the foregoing amendment, claims 15 and 19 have been amended to recite that the composition is a composition for inhibiting tumors. Support for the amendment to the claims is found throughout the specification as filed.

Claims 16-18 and 20 have been amended to recite "The" rather than "A" at the beginning of the claim. Furthermore, new claims 21-24 have been added.

Support for new claims 21 and 24 is found at, e.g., page 3, line 32, to page 4, line 26; and page 10, lines 20-21. Support for new claims 22 and 23 is found at, e.g., page 10, lines 25-27, and at page 12, lines 2-3. No new matter has been added by the foregoing amendment.

Rejection of Claims 15-18 Under 35 U.S.C. § 103(a)

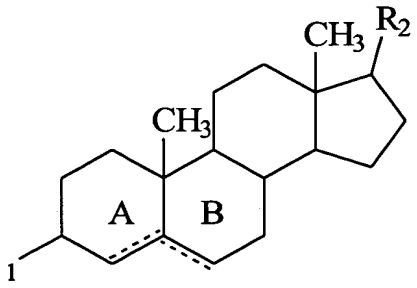
Claims 15-18 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over Adams et al (*Cancer Research 38*:4036-4040 (1978)) taken with Peat (U.S. Patent No. 4,628,052). For the reasons set forth below, withdrawal of this rejection under 35 U.S.C. § 103(a) is believed to be in order.

Δ5-Androstenediol (AED) is a naturally-occurring metabolite of dehydroepiandrosterone (DHEA), the most abundant product of the adrenal glands. AED may also arise from the metabolism of other steroids. AED exists in two epimeric forms:

Δ5-Androstene-3-β,17α-diol (αAED) and Δ5-Androstene-3-β,17β-diol (βAED). Both are naturally occurring metabolites of dehydroepiandrosterone (DHEA).

Until the present invention, the beneficial effects of αAED for inhibiting tumor growth had not been appreciated. The present inventor discovered those beneficial effects, and thus the present invention is drawn to a novel composition of matter for inhibiting tumors comprising 5-androstene-3β, 17α-diol (αAED) or another compound encompassed by the claimed invention (see claim 15).

Peat discloses the use of compounds, such as DHEA, iso-androsterone, etiocholanolone, progesterone and pregnenolone, and other anesthetic steroids, for the treatment of arthritis and other joint disabilities. Peat indicates that a prefered anesthetic steroid is selected from compounds of the formula (I):



wherein R_1 is O or OH and R_2 is O, OH or $COCH_3$; and which may contain one double bond in ring A and/or ring B. Although Peat does disclose that the 17 keto is converted to a hydroxyl group, Peat does not differentiate between the isomers. There is no indication as to whether the hydroxyl group is in the alpha or beta position. In other words, Peat does not teach or suggest that it is possible to induce the different physiological effects by

varying between an alpha and beta isomer, nor does that reference teach or suggest the particular effects attributable to the 17 alpha and 17 beta isomers of androstenediol.

The beta and alpha isomers of androstenediol function in opposition of each other. For example, βAED up-regulates immunity, whereas αAED induces apoptosis, i.e., programmed cell death, but only in tumor cells. Additionally, αAED increases the levels of the proinflammatory nuclear factor, NF-κB, whereas βAED reduces the levels of NF-κB. Since these isomers of androstenediol function in opposition of each other, it is hard to conclude that Peat discloses or suggests the present invention, which requires that the group at the 17 position be in the alpha position.

Peat does not disclose or suggest that 5-androstene-3β, 17α-diol (αAED) has biological activity, and thus could not possibly disclose or suggest the use of this compound in the claimed pharmaceutical formulation.

Adams et al does not solve the deficiencies of Peat. Adams et al discloses that DHEA is metabolized by human mammary tumors *in vitro* to 5-androstene-3β, 17β-diol (βAED), which then competes with the estrogen receptor. However, Adams et al discloses on page 4039, column 1, lines 15-16, that "it remains to be seen whether such translocations [of the estrogen receptor] are accompanied by a biological response." Adams et al further discloses at line 29 "in our experience with some 15 tumors incubated with labeled DHEA of high specific activity, no conversions to estrogen could be detected." Thus, Adams et al does not show any biological response to 5-androstene-3β, 17β-diol (βAED), let alone to 5-androstene-3β, 17α-diol (αAED), and clearly does not report any anti-tumor effects.

In fact, previous findings by the applicant specifically demonstrate that the anti-tumor effects of 5-androstene 3β, 17α-diol (αAED) in human breast cancer cells is independent of either the estrogen or the androgen receptor (see Hynh P.N. et al, *Cancer Detection and Prevention 24(5)*:435-445 (2000), attached hereto as Exhibit A). This would negate any possible interpretation of Adams et al which would suggest that 5-androstene 3β, 17α-diol (αAED) competes with the estrogen receptor.

Adams et al does not disclose or suggest that 5-androstene-3β, 17α-diol (αAED) has biological activity, and therefore does not disclose or suggest the use of this compound in the claimed pharmaceutical formulation.

Neither Adams et al nor Peat discloses or suggests the use of 5-androstene-3β, 17α-diol (αAED), or any of the compounds encompassed by the present invention. Likewise, neither reference discloses or suggests such compounds in a composition for inhibiting tumors. Thus, even if those references were taken together, the references would not disclose or suggest the claimed invention. The present invention is not obvious in view of Adams et al taken together with Peat.

In light of these remarks, applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 103(a).

Rejection of Claims 15-20 Under 35 U.S.C. § 112, Second Paragraph

Claims 15-20 have been rejected under 35 U.S.C. § 112, second paragraph, for purportedly being indefinite. For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

According to the Examiner, the claims are indefinite for failing to recite the intended application of the claimed composition. By the present amendment, the claims have been amended to recite that the claimed composition is used for inhibiting tumors. In light of this amendment to the claims, applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

In the event that there are any questions relating to this application, the Examiner is invited to telephone the undersigned so that prosecution of the subject application may be expedited.

Respectfully submitted,

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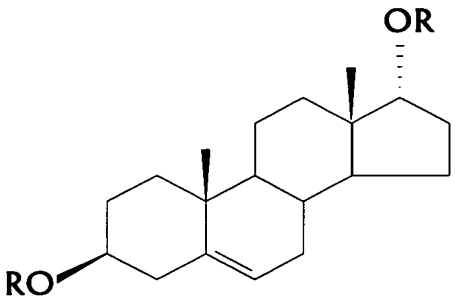
Attachment to Amendment and Reply dated January 7, 2002

Marked-up Claims 15-20

15. (Three Times Amended) A composition of matter for inhibiting tumors comprising [an] a tumor inhibiting effective amount of 5-androstene-3β,17α- diol or an ester or ether thereof of the formula:



wherein R [may be] is selected from a group consisting of H, alkenyl of 2-8 carbons, alkyl of 1-8 carbons, phenylalkyl of 1-4 carbons, phenyl [or] and COR_2,wherein R_2 [may be] is selected from a group consisting of H, alkyl of 1-8 carbons, alkenyl of 2-8 carbons, phenylalkyl wherein the alkyl has 1-4 carbons (including benzyl) [or R_2 may be] and phenyl, and wherein any phenyl moiety may have up to three substituents [chosen from among] selected from the group consisting of hydroxy, carboxy of 1-4 carbons, halo, alkoxy of 1-4 carbons, alkyl of 1-4 carbons, [or] and alkenyl of 2-4 carbons and wherein

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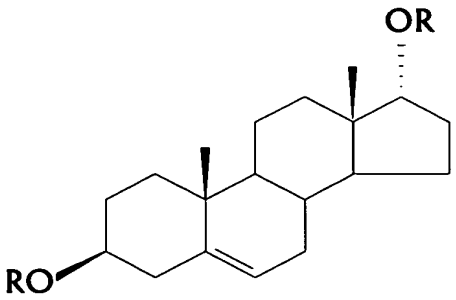
any alkyl may be a straight chain, branched chain, or the alkyl may be wholly or partially cyclized, [in a pharmaceutically acceptable carrier,] said formulation being in the form of a capsule or tablet.

16. (Amended) [A] The composition of claim 15 wherein the composition contains 5-androstene-3β, 17α-diol.

17. (Amended) [A] The composition of claim 15 in the form of a tablet.

18. (Amended) [A] The composition of claim 15 in the form of a capsule.

19. (Three Times Amended) A composition of matter for inhibiting tumors comprising [an] a tumor inhibiting effective amount of 5-androstene-3β,17α- diol or an ester or ether thereof of the formula:



Attachment to Amendment and Reply dated January 7, 2002

Marked-up Claims 15-20

wherein R [may be] is selected from a group consisting of H, alkenyl of 2-8 carbons, alkyl of 1-8 carbons, phenylalkyl of 1-4 carbons, phenyl [or] and COR_2,wherein R_2 [may be] is selected from a group consisting of H, alkyl of 1-8 carbons, alkenyl of 2-8 carbons, phenylalkyl wherein the alkyl has 1-4 carbons (including benzyl) [or R_2 may be] and phenyl, and wherein any phenyl moiety may have up to three substituents [chosen from among] selected from the group consisting of hydroxy, carboxy of 1-4 carbons, halo, alkoxy of 1-4 carbons, alkyl of 1-4 carbons, [or] and alkenyl of 2-4 carbons and wherein any alkyl may be a straight chain, branched chain, or the alkyl may be wholly or partially cyclized, in a pharmaceutically acceptable carrier, wherein said 5-androstene-3β,17α- diol or ester or ether thereof is part of a cyclodextrin inclusion complex.

20. (Amended) [A] The composition of claim 19 wherein the composition contains 5-androstene-3β, 17α-diol.